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Disease Progression in Nonintervened Saphenous Vein Graft Segments

A Serial Intravascular Ultrasound Analysis

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Objectives We used serial intravascular ultrasound (IVUS) to assess disease progression in nonintervened saphenous vein graft (SVG) segments to determine the natural rate of disease progression in SVG.

Background There are no serial IVUS studies of disease progression or luminal compromise in SVGs.

Methods We assessed serial (baseline and follow-up at 16.2 ± 7.4 months) IVUS findings in 50 nonintervened SVG segments in 44 patients. The SVG age was 13.5 ± 3.6 years.

Results Overall, from baseline to follow-up, plaque area increased ($\Delta = +0.58 \pm 1.25$ mm^2, $p = 0.003$), and SVG and minimum lumen area (MLA) decreased ($\Delta = -0.50 \pm 1.14$ mm^2, $p = 0.002$, and $\Delta = -1.08 \pm 1.28$ mm^2, $p < 0.001$, respectively). The MLA decreased in 34 lesions ($\Delta = -1.67 \pm 1.08$ mm^2), and MLA increased in 16 lesions ($\Delta = +0.19 \pm 0.47$ mm^2). Compared with lesions with an increase in MLA, lesions with a decrease in MLA were associated with: 1) larger baseline SVG and plaque areas and plaque burden (15.57 ± 3.90 mm^2 vs. 11.55 ± 2.30 mm^2, $p < 0.001$; 7.97 ± 3.77 mm^2 vs. 4.27 ± 1.92 mm^2, $p < 0.001$; and 48.7 ± 14.2% vs. 36.0 ± 13.4%, $p = 0.004$, respectively); and 2) a greater decrease in SVG area ($\Delta = -0.96 \pm 1.05$ mm^2 vs. $+0.48 \pm 0.58$ mm^2, $p < 0.001$) and greater increase in plaque area ($\Delta = +0.71 \pm 1.47$ mm^2 vs. $+0.29 \pm 0.45$ mm^2, $p < 0.001$). The ΔMLA correlated with both Δplaque area ($r = -0.589$, $p < 0.001$) and ΔSVG area ($r = 0.470$, $p = 0.001$), and Δplaque area correlated with ΔSVG area ($r = 0.436$, $p = 0.002$). There were linear relations between both the Δplaque area ($r = 0.519$, $p < 0.001$) and Δlumen area ($r = -0.500$, $p < 0.001$) versus follow-up low-density lipoprotein (LDL) cholesterol; a follow-up LDL cholesterol of 100 mg/dl predicted no plaque increase.

Conclusions Lumen loss in nonintervened SVG segments correlated with an increase in plaque area and a decrease in SVG area (plaque growth and negative remodeling) with a linear relationship between plaque growth versus follow-up LDL cholesterol leading to long-term lumen loss. (J Am Coll Cardiol 2009;53:1257–64) © 2009 by the American College of Cardiology Foundation

Atherosclerosis imaging has contributed to the understanding of the natural history of coronary artery disease, including the processes leading to luminal narrowing and the assessment of disease burden and therapeutic efficacy. Serial intravascular ultrasound (IVUS) is now being used to study plaque progression and regression (1–13), in part because of successful studies of restenosis and transplant vasculopathy. With IVUS, changes in lumen dimensions in nonintervened segments in native coronary arteries can be separated into an increase or decrease in vessel area and/or an increase or decrease in plaque area (1–8,14–19). However, to the best of our knowledge, no studies have examined disease progression or luminal compromise in nonintervened saphenous vein bypass graft (SVG) lesions. Therefore, the purpose of the present study was to use serial (baseline and follow-up) IVUS to assess disease progression in nonintervened SVG segments.

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Methods

Patient population. We identified 44 patients who underwent baseline and follow-up IVUS imaging of a nonintervened SVG segment at the Washington Hospital

Abbreviations and Acronyms

IVUS = intravascular ultrasound
LDL = low-density lipoprotein
MLA = minimum lumen area
SVG = saphenous vein graft

Center. At baseline, all segments had a minimum lumen area (MLA) >4.0 mm^2 and a plaque burden <0.75 and were not treated with percutaneous coronary intervention. Hospital records of all the patients were reviewed to obtain information on clinical demographic data and medical history. This study was performed with the approval of the institutional review board.

IVUS imaging and analysis. The IVUS examinations were performed at baseline and at follow-up after intra-SVG administration of 200 μg nitroglycerin with a commercially available IVUS system (Boston Scientific Corporation/SCIMed, Minneapolis, Minnesota). The IVUS catheter was advanced distal to the target lesion, and imaging was performed retrograde to the aorto-ostial junction at an automatic pullback speed of 0.5 mm/s.

The IVUS analyses were performed according to the American College of Cardiology Clinical Expert Consensus Document on Standards for Acquisition, Measurement and Reporting of Intravascular Ultrasound Studies (20). Quantitative IVUS measurements were performed with planimetry software (TapeMeasure, INDEC Systems Inc., Mountain View, California) and included SVG area, lumen area, plaque (SVG − lumen) area, and plaque burden (plaque area/SVG area). The same anatomic image slices were analyzed at baseline and at follow-up using axial landmarks and the known pullback speed of the transducer. The anatomic image slices selected for serial analysis had an axial location at the smallest follow-up MLA site and at the follow-up proximal and distal reference segments (single slices with the largest lumen and smallest plaque burden within 10 mm proximally and distally to the follow-up MLA site but before any large side branch). Soft plaque was less bright than the adventitia, fibrotic plaque was as bright as or brighter than the adventitia without acoustic shadowing, and calcific plaque was brighter than the adventitia with acoustic shadowing. When there was no dominant plaque composition, the plaque was classified as mixed. Remodeling index was the ratio of the lesion site SVG cross-sectional area divided by the average of the proximal and distal reference SVG cross-sectional area (21).

Statistical analysis. The Statistical Package for Social Sciences for Windows version 15.0 (SPSS Inc., Chicago, Illinois) was used for all analyses. Continuous variables were presented as the mean value ± 1 SD and compared by paired or unpaired Student *t* test or nonparametric Wilcoxon signed-rank test if normality assumption was violated. Discrete variables are presented as percentages and relative frequencies. Linear regression analysis was used to evaluate the associations among lumen area versus plaque area and SVG area, between SVG area versus plaque area, and between plaque area and lumen area versus follow-up low-density lipoprotein (LDL) cholesterol. All analysis was done on an SVG level and not a patient level. A value of $p < 0.05$ was considered statistically significant.

Results

Baseline characteristics. Baseline characteristics are summarized in Table 1. The SVG age was 13.5 ± 3.6 years, and the interval between IVUS studies was 16.2 ± 7.4 months. One-third of the patients had diabetes mellitus, more than two-thirds of the patients had hypertension, and more than two-thirds of the patients took statins.

Serial IVUS results. Serial IVUS results are shown in Table 2. From baseline to follow-up, reference segment plaque area increased and SVG and lumen areas decreased. From baseline to follow-up, lesion site plaque area increased ($\Delta = +0.58 \pm 1.25$ mm^2) and SVG and lumen areas decreased ($\Delta = -0.50 \pm 1.14$ mm^2 and $\Delta = -1.08 \pm 1.28$ mm^2, respectively). The remodeling index also decreased from baseline to follow-up, but plaque morphology did not change. The Δlumen area correlated with both Δplaque area ($r = -0.589$, $p < 0.001$) and ΔSVG area ($r = 0.470$, $p = 0.001$), and Δplaque area correlated with ΔSVG area ($r = 0.436$, $p = 0.002$) (Fig. 1). When patients were divided into 2 groups according to a follow-up duration >12 and <12

Table 1 Baseline Clinical Characteristics

Time of follow-up (months)	16.2 ± 7.4
Graft age (yrs)	13.5 ± 3.6
Age (yrs)	64.5 ± 12.8
Male	34 (77.3)
Clinical presentation	
Stable angina	8 (18.2)
Unstable angina	32 (72.7)
NSTEMI	4 (9.1)
Diabetes mellitus	14 (31.8)
Hypertension	30 (68.2)
Smoking	13 (29.5)
Family history of coronary artery disease	10 (22.7)
Left ventricular ejection fraction (%)	39 ± 15
Total cholesterol (mg/dl)	203 ± 128
LDL cholesterol (mg/dl)	126 ± 39
HDL cholesterol (mg/dl)	39 ± 15
Triglycerides (mg/dl)	184 ± 120
Medications	
Statins	34 (77.3)
Beta-blockers	33 (75.0)
Angiotensin-receptor antagonists	24 (54.5)
Clopidogrel	44 (100.0)
Diseased vessel (n = 50)	
SVG to LAD	13 (26.0)
SVG to LCX	21 (42.0)
SVG to RCA	16 (32.0)

Data are presented as n (%) of patients or mean ± SD.

HDL = high-density lipoprotein; LAD = left anterior descending artery; LCX = left circumflex artery; LDL = low-density lipoprotein; NSTEMI = non–ST-segment elevation myocardial infarction; RCA = right coronary artery.

Table 2 Serial Intravascular Ultrasound Data

	Baseline	Follow-Up	p Value
Reference			
SVG area (mm^2)	14.02 ± 3.68	13.68 ± 3.37	0.023
Lumen area (mm^2)	9.45 ± 2.59	8.56 ± 2.23	0.008
Plaque area (mm^2)	4.57 ± 1.66	5.12 ± 2.18	0.016
Plaque burden (%)	32.6 ± 13.8	37.4 ± 11.2	0.012
Smallest follow-up MLA site			
SVG area (mm^2)	14.28 ± 3.93	13.78 ± 3.37	0.003
Lumen area (mm^2)	7.50 ± 1.65	6.42 ± 2.04	<0.001
Plaque area (mm^2)	6.79 ± 3.71	7.37 ± 3.70	0.002
Plaque burden (%)	44.6 ± 15.1	50.9 ± 17.7	<0.001
Remodeling index	1.019 ± 0.286	1.007 ± 0.128	0.032
Plaque morphology			0.12
Soft	34 (68)	29 (58)	
Fibrotic	10 (20)	15 (30)	
Calcific	4 (8)	5 (10)	
Mixed	2 (4)	1 (2)	

Data are presented as n (%) of patients or mean ± SD.
MLA = minimum lumen area; SVG = saphenous vein graft.

months, there were no significant differences in Δplaque area and Δplaque burden between lesions with a follow-up duration >12 months (14 to 25 months, n = 29) and lesions with a follow-up duration <12 months (2 to 11 months, n = 21) (Δ = +0.66 ± 1.43 mm^2 vs. Δ = +0.52 ± 0.99 mm^2, p = 0.322; and Δ = +7.6 ± 7.7% vs. Δ = +4.5 ± 7.3%, p = 0.160, respectively).

Differences between lesions with a decrease in MLA and those with an increase in MLA. We analyzed the cross-section located at the follow-up MLA site. The MLA decreased in 34 lesions (mean Δ = −1.67 ± 1.08 mm^2), and MLA increased in 16 lesions (mean Δ = +0.19 ± 0.47 mm^2). Baseline clinical characteristics according to an increase versus a decrease in MLA are shown in Table 3. Other than male predominance and a trend toward more unstable clinical presentation in lesions with a decrease in MLA, there were no differences between the 2 groups.

Baseline and follow-up IVUS findings according to an increase versus a decrease in MLA are shown in Table 4. Compared with lesions with an increase in MLA at follow-up, lesions with a decrease in MLA were associated with larger baseline SVG and plaque areas and plaque burden and with a greater decrease in SVG area and a greater increase in plaque area during follow-up.

Relationship between Δplaque area and Δlumen area versus follow-up LDL cholesterol. There were linear relations between both Δplaque area (r = 0.519, p < 0.001) and Δlumen area (r = −0.500, p < 0.001) versus follow-up LDL cholesterol. With regression analysis, the cutoff value of follow-up LDL cholesterol that best predicted no plaque area increase was 100 mg/dl (Fig. 2).

When patients were divided into 2 groups according to follow-up LDL cholesterol above and below 100 mg/dl, there were no significant differences in the baseline IVUS variables between lesions with follow-up LDL cholesterol

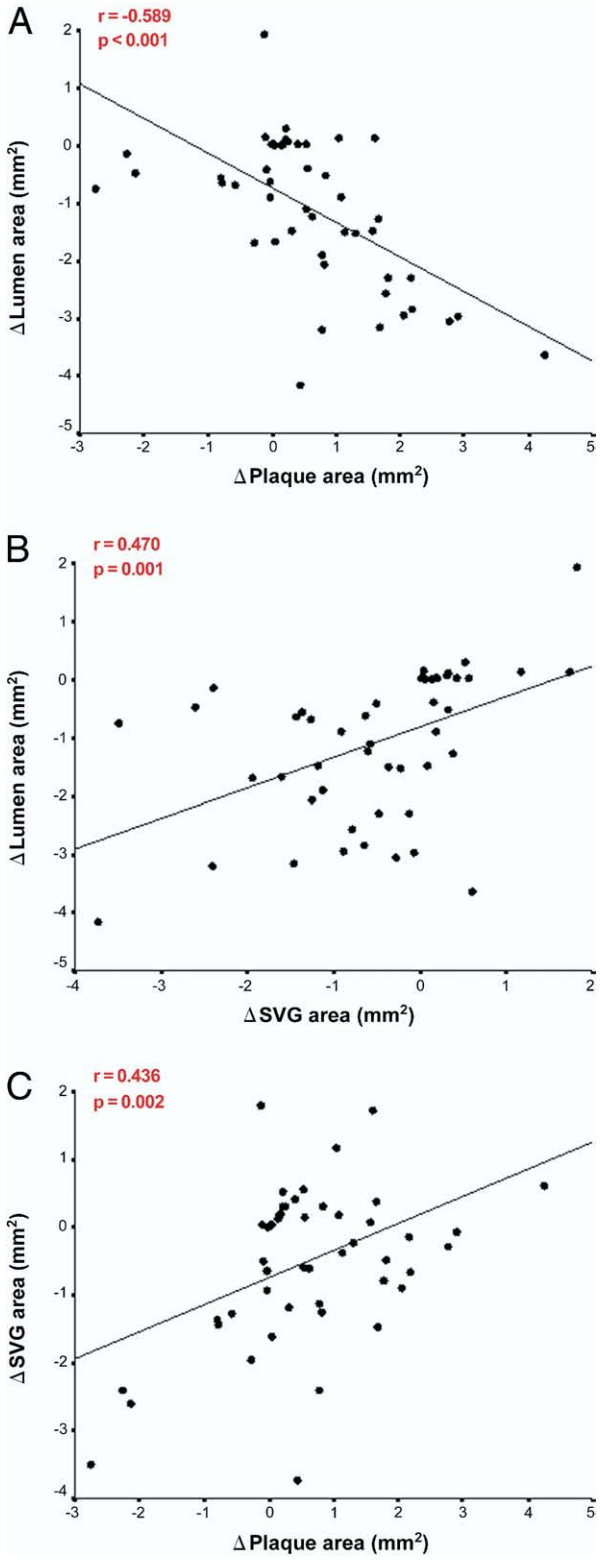

Figure 1 IVUS Measurement Correlations

The correlation between Δlumen area versus Δplaque area **(A)**, between Δlumen area versus Δsaphenous vein graft (SVG) area **(B)**, and between ΔSVG area versus Δplaque area **(C)**.

Table 3 Baseline Clinical Characteristics According to Increase/Decrease in MLA

	Decrease in MLA (n = 34)	Increase in MLA (n = 16)	p Value
Time of follow-up (months)	16.6 ± 8.2	15.8 ± 7.0	0.2
Graft age (yrs)	13.8 ± 3.9	13.3 ± 3.0	0.2
Age (yrs)	65.5 ± 13.3	63.6 ± 10.2	0.2
Male	29 (85.3)	9 (56.3)	0.025
Clinical presentation			0.080
Stable angina	5 (14.7)	4 (25.0)	
Unstable angina	28 (82.4)	9 (56.3)	
NSTEMI	1 (2.9)	3 (18.8)	
Diabetes mellitus	24 (70.6)	9 (56.3)	0.3
Hypertension	24 (70.6)	9 (56.3)	0.3
Smoking	11 (32.4)	2 (12.5)	0.14
Family history of coronary artery disease	8 (23.5)	3 (18.8)	0.7
Left ventricular ejection fraction (%)	39 ± 15	39 ± 15	
Total cholesterol (mg/dl)	209 ± 136	188 ± 112	0.2
LDL cholesterol (mg/dl)	130 ± 41	125 ± 28	0.4
HDL cholesterol (mg/dl)	38 ± 14	40 ± 17	0.4
Triglycerides (mg/dl)	188 ± 126	180 ± 115	0.3
Diseased vessel			0.11
SVG to LAD	6 (17.6)	7 (43.8)	
SVG to LCX	17 (50.0)	4 (25.0)	
SVG to RCA	11 (32.4)	5 (31.3)	

Data are presented as n (%) of patients or mean ± SD.
Abbreviations as in Tables 1 and 2.

≥100 mg/dl (n = 31) and lesions with follow-up LDL cholesterol <100 mg/dl (n = 19) (Table 5). Lesions with follow-up LDL cholesterol ≥100 mg/dl had a greater increase in plaque area and a greater decrease in lumen area compared with lesions with follow-up LDL cholesterol <100 mg/dl at follow-up (Fig. 3). Plaque regressed in 13 lesions (26% of the lesions) at follow-up, and this plaque regression was observed more frequently in lesions with follow-up LDL cholesterol <100 mg/dl compared with lesions with follow-up LDL cholesterol ≥100 mg/dl (63.2% vs. 16.1%, p = 0.001).

Table 4 Baseline and Follow-Up Intravascular Ultrasound Findings According to Increase/Decrease in MLA

	Decrease in MLA (n = 34)	Increase in MLA (n = 16)	p Value
Baseline SVG area (mm^2)	15.57 ± 3.90	11.55 ± 2.30	<0.001
Baseline MLA (mm^2)	7.60 ± 1.56	7.28 ± 1.85	0.524
Baseline plaque area (mm^2)	7.97 ± 3.77	4.27 ± 1.92	<0.001
Baseline plaque burden (%)	48.7 ± 14.2	36.0 ± 13.4	0.004
Follow-up SVG area (mm^2)	14.61 ± 3.46	12.03 ± 2.44	0.004
Follow-up MLA (mm^2)	5.93 ± 1.84	7.47 ± 2.10	0.011
Follow-up plaque area (mm^2)	8.69 ± 3.59	4.56 ± 2.01	<0.001
Follow-up plaque burden (%)	57.5 ± 15.4	37.0 ± 14.0	<0.001
ΔSVG area (mm^2)	−0.96 ± 1.05	0.48 ± 0.58	<0.001
ΔMLA (mm^2)	−1.67 ± 1.08	0.19 ± 0.47	<0.001
Δplaque area (mm^2)	0.71 ± 1.47	0.29 ± 0.45	<0.001
Δplaque burden (%)	8.8 ± 8.0	1.1 ± 2.9	<0.001

Data are presented as mean ± SD.
Abbreviations as in Table 2.

When patients were divided into 2 groups according to statin therapy, there were no significant differences in the baseline IVUS variables between statin-treated lesions (n = 40) and nonstatin-treated lesions (n = 10) (Table 5), but there was a smaller increase in plaque area in statin-treated lesions compared with nonstatin-treated lesions. The SVG area decreased (negative remodeling) in both statin-treated

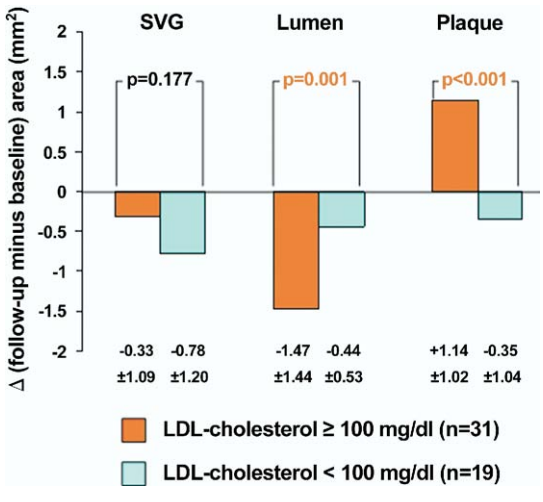

Figure 2 Effect of LDL Cholesterol

Changes of saphenous vein graft (SVG) area, lumen area, and plaque area in lesions with low-density lipoprotein (LDL) cholesterol ≥100 mg/dl versus lesions with LDL cholesterol <100 mg/dl.

Table 5 Baseline Intravascular Ultrasound Findings According to the Follow-Up LDL Cholesterol Levels and Statin Therapy

	Follow-Up LDL Cholesterol ≥100 mg/dl (n = 31)	Follow-Up LDL Cholesterol <100 mg/dl (n = 19)	p Value
Baseline SVG area (mm^2)	14.57 ± 3.41	13.82 ± 4.72	0.548
Baseline MLA (mm^2)	7.82 ± 1.82	6.96 ± 1.17	0.073
Baseline plaque area (mm^2)	6.75 ± 3.39	6.85 ± 4.27	0.930
Baseline plaque burden (%)	44.3 ± 15.3	45.2 ± 15.0	0.825
	Statin (n = 40)	**No Statin (n = 10)**	**p Value**
Baseline SVG area (mm^2)	14.31 ± 3.97	14.17 ± 3.97	0.917
Baseline MLA (mm^2)	7.49 ± 1.81	7.53 ± 0.71	0.902
Baseline plaque area (mm^2)	6.83 ± 3.71	6.63 ± 3.90	0.885
Baseline plaque burden (%)	45.1 ± 14.7	42.6 ± 17.3	0.646

Data are presented as mean ± SD.
Abbreviations as in Tables 1 and 2.

and nonstatin-treated lesions; however, this was not statistically significant between statin-treated and nonstatin-treated lesions (Fig. 4). There were no differences in plaque area change, lumen area change, and SVG area change according to type of statin. When we compared the plaque area change, lumen area change, and SVG area change according to the dose of statin (high-dose group [n = 18, 60 to 80 mg/day] vs. usual dose group [n = 32, <40 mg/day]), plaque area decreased in the high-dose group and increased in the usual-dose group (−0.23 ± 1.15 mm^2 vs. +1.03 ± 1.35 mm^2, $p < 0.001$). Plaque regression was observed more frequently in the high-dose group compared with usual-dose group (55.6% vs. 9.4%, $p < 0.001$).

There were no associations between Δplaque area and follow-up high-density lipoprotein cholesterol ($p = 0.6$), diabetes mellitus ($p = 0.3$), or hypertension ($p = 0.3$).

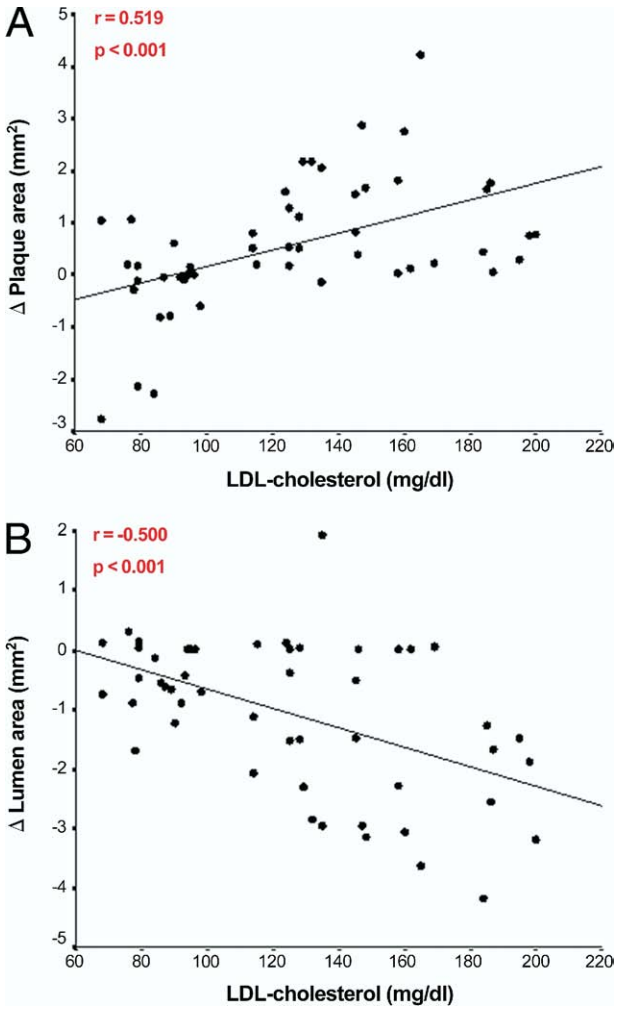

Figure 3 Correlation With LDL Cholesterol

The correlation between plaque area and low-density lipoprotein (LDL) cholesterol **(A)** and between lumen area and LDL cholesterol **(B)**.

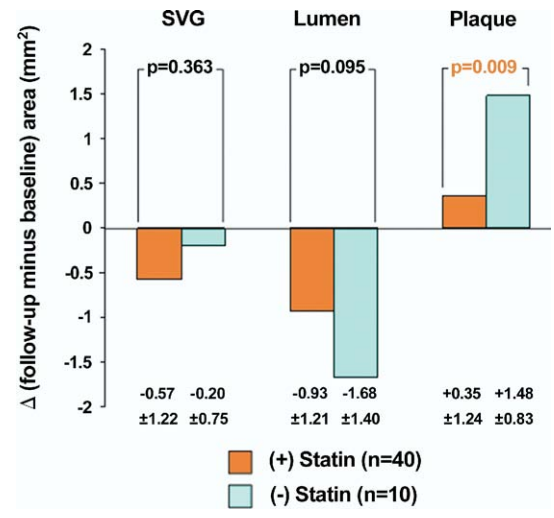

Figure 4 Effect of Statin Use

Changes of saphenous vein graft (SVG) area, lumen area, and plaque area according to the statin therapy.

Discussion

The present serial IVUS study of nonintervened SVG segments showed the following: 1) plaque area increased, and SVG and lumen area decreased from baseline to follow-up; 2) lesions with a decrease in MLA at follow-up were associated with larger baseline SVG and plaque areas and with a greater decrease in SVG area and a greater increase in plaque area during follow-up; 3) change in lumen area correlated with both changes in plaque area and SVG area; 4) change in plaque area correlated with a change in SVG area; 5) there were linear relations between both changes in the plaque area and lumen area versus follow-up LDL cholesterol with a cutoff value of follow-up LDL cholesterol of 100 mg/dl predicting no plaque area increase; and 6) there was a smaller increase in plaque area in statin-treated lesions compared with nonstatin-treated lesions. These findings are remarkably similar to serial IVUS findings in native coronary arteries.

Serial angiography has been used to study SVG disease progression. Rodes-Cabau et al. (22) reported that significant angiographic disease progression occurred in 48% of SVG lesions. Domanski et al. (23) reported that the severity of the SVG stenosis and the size of the SVG lumen diameter at baseline angiography were predictive of angiographic SVG atherosclerosis progression. Campos et al. (24) presented long-term follow-up data of normal and minimally diseased SVGs; more than one-half of these grafts remained normal or minimally diseased at follow-up. Mehta et al. (25) also showed a favorable outcome if SVGs were normal at baseline.

Compared with IVUS—which provides a tomographic, transmural view and can directly visualize and measure atherosclerotic plaque—angiography visualizes only lumen dimension and can only indirectly estimate the severity of atherosclerotic plaque. In angiographically normal SVGs, IVUS and pathological studies have shown a doubling of intimal thickness (26) and total wall thickness (27) by the end of the first post-operative year. However, to date (and unlike native coronary artery disease) there have been no published serial IVUS data on SVG disease progression and, especially, the relationship between progression and baseline findings. In the current study Δlumen area correlated almost equally with ΔSVG and Δplaque areas, whereas in native coronary arteries Δlumen area correlated more with Δexternal elastic membrane area than with Δplaque area.

In transplant studies, changes in plaque burden and remodeling response were time-dependent. With multislice computed tomography angiography, Lau et al. (28) reported that lumen loss in SVG between post-operative months 1 and 12 is predominantly caused by negative remodeling of the whole vessel rather than by changes in wall thickness. Tsutsui et al. (11) compared the late disease process of transplant vasculopathy between coronary segments with early constrictive and expansive remodeling. In their study (11), annual changes in intimal area were similar between segments with early constrictive remodeling and expansive remodeling throughout the follow-up period; however, during the second and third year, annual increases in external elastic membrane area were greater in segments with early constrictive remodeling than in segments with early expansive remodeling. Despite this late expansion, segments with early constrictive remodeling showed a cumulative decrease in the external elastic membrane area and a greater lumen loss than segments with early expansive remodeling. In the present study, which enrolled small numbers of patients with short follow-up duration, the grafts were approximately 1 decade old and were imaged approximately 16 months apart, and there were no significant differences in plaque area change and plaque burden change between lesions with a follow-up duration >12 months and lesions with a follow-up duration <12 months. Optimally, serial studies of bypass grafts with IVUS imaging at more than 2 time points would provide further insight.

Impact of statin therapy and serum follow-up LDL cholesterol on disease progression. Serial IVUS studies have been used to evaluate the effect of pharmacology on plaque progression or regression in native coronary arteries (29–38). In the present study, there was a smaller increase in SVG plaque area in statin-treated lesions compared with nonstatin-treated lesions, similar to findings in native coronary arteries. Serial IVUS studies have also been used to study the relationship between plaque progression or regression in native coronary arteries and serum LDL cholesterol levels (14,30,32–38). In these studies, the cutoff value of LDL cholesterol that was associated with either no change or a decrease in plaque area was <100 mg/dl. The results of the present study were similar to those of the previous studies in native coronary arteries (14,30,33–38).

Angiographic but not IVUS studies have reported the relationship of statin therapy and lipid-lowering on atherosclerosis progression in SVGs. The Post-CABG (Post Coronary Artery Bypass Graft) trial investigators (39) reported that 27% of patients treated with an aggressive LDL cholesterol-lowering regimen had SVG disease progression versus 39% of patients treated with a moderate LDL cholesterol-lowering regimen. Goldman et al. (40) reported that lower serum cholesterol was a significant predictor of graft patency in the VA Cooperative Studies Trial. Domanski et al. (23) reported that high LDL cholesterol was an independent predictor for SVG atherosclerosis progression in the CABG trial. Rodes-Cabau et al. (22) reported that low high-density lipoprotein cholesterol was associated with SVG atherosclerosis progression. Knatterud et al. (41) reported a 24% reduction in composite clinical end points in patients assigned to an aggressive strategy (LDL cholesterol levels <100 mg/dl) compared with patients assigned to a moderate strategy (LDL cholesterol levels 132 to 136 mg/dl) during 7.5

years of follow-up in the CABG trial. In the present study there was a linear relationship between the change of plaque area versus follow-up LDL cholesterol; the cutoff value of follow-up LDL cholesterol of 100 mg/dl was associated with no plaque area increase with a trend toward less progression in statin-treated patients. Our results also suggest that serial IVUS study can be used to evaluate SVG progression/regression and assess the effects of pharmacotherapy and risk factors, which is similar to findings in native coronary arteries.

Remodeling. With IVUS, remodeling can be assessed both at a single time point and serially. At a single time point, the remodeling index is derived by comparing lesion vessel cross-sectional area with the reference (42). With serial IVUS examinations, remodeling can be assessed as the increase or decrease in vessel area; positive serial remodeling can be defined as an increase of vessel area; in contrast, negative or intermediate serial remodeling can be defined as a decrease or no change of vessel area (18,19).

Remodeling is a well-established phenomenon in native coronary arteries; however, the presence of remodeling within SVGs is controversial. Nishioka et al. (43) reported a lack of remodeling in SVGs; however, this conclusion was disputed by other authors (44–46). In the present serial IVUS study, lumen loss in nonintervened SVG segments was associated with negative remodeling (decrease in SVG area) from baseline to follow-up; furthermore, the change in SVG area correlated with the change in plaque area. Again, these results are remarkably similar to those in native coronary arteries and indicate that SVGs undergo remodeling just like native arteries.

Study limitations. First, this study is based on a small sample size, was retrospective, and was from a single center. Second, we were able to include only patients with significant SVG disease who were admitted for repeat cardiac revascularization and not patients soon after surgery. Therefore, the findings of the present study might not be applicable to the general population. Third, the present study is based on the serial comparison of measurements in single-image slices, an approach validated in many initial IVUS studies. However, because of limitations of matching, some studies use volumetric analysis by integrating several slices along entire coronary segments. Fourth, plaque morphology was assessed visually with grayscale IVUS; however, this conventional IVUS has significant limitations in assessing plaque composition. At present, radiofrequency analysis has become available for further plaque characterization but has not yet been validated in SVGs. Fifth, our mean follow-up period was only 16 months, and we did not collect longer-term IVUS follow-up data. Lastly, the population was a relatively high-risk group (prevalence of diabetes mellitus at 31.8% and left ventricular ejection fraction at 39%), so the results should only be applied to the population studied.

Conclusions

Lumen loss in nonintervened SVG segments was associated with an increase in plaque area and a decrease in SVG area (plaque growth and negative remodeling). Importantly, there was a linear relationship between follow-up LDL cholesterol and plaque growth leading to lumen loss during follow-up.

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